

## APPENDIX A

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APR 01 2002

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26. An implant composition comprising:

10 a first component comprising a biologically active composition contained in a first delivery vehicle capable of immediately releasing said biologically active composition upon implantation in an animal body and which is selected from the group consisting of encapsulants where the coating wall material is highly soluble in body fluids, porous or freeze-dried solid compositions, solid tablets or pellets containing a disintegrating agent which causes the solid tablet or pellet to rapidly break down when in body fluids, solid tablets or pellets containing said biologically active material in fine or micronized particle sizes and mixtures thereof; and

15 (b) a second component comprising the same biologically active composition as in component (a) contained in a second delivery vehicle capable of releasing said biologically active composition on a sustained basis upon implantation in an animal body and which is selected from the group consisting of encapsulated solutions or suspensions, biodegradable solid substances, conventional tablet/pellet ingredients, conventional tablet/pellet ingredients coated with a polymeric membrane to control release, conventional tablets or pellets  
20 containing said biologically active material having large particle sizes, matrix-tablets based on gel-forming excipients, matrix-type systems based on non-biodegradable polymers, membrane-type systems based on non-biodegradable polymers, matrix-type systems based on biodegradable polymers, matrix-type systems implant based on lipidic excipients, and mixtures thereof;

25 wherein said implant composition is implanted in an animal body by injection.

27. The implant composition of claim 26 wherein the first delivery vehicle comprises solid tablets or pellets containing a disintegrating agent and wherein the second vehicle comprises solid tablets or  
30 pellets not containing a disintegrating agent.

28. The implant composition of Claim 27, wherein said disintegrating agent is selected from the group consisting of sodium crosscarmellose, microcrystalline cellulose, sodium carboxymethyl-cellulose, alginic acid, starch, potassium polacrilin, colloidal silicon dioxide, crospovidone, guar gum,  
35 magnesium aluminum silicate, methyl cellulose, powdered cellulose, pregelatinized starch, sodium starch glycolate and sodium alginate and mixtures thereof.

29. The implant composition of Claim 26 wherein said biologically active composition is selected from the group consisting of enzymes or other organic catalysts, ribozymes, organometallics, proteins and glycoproteins, peptides, poly(amino acids), antibodies, nucleic acids, steroids, antibiotics, antimycotics, anti-narcotics, cytostatics, cytotoxics, cytokines, carbohydrates, oleophobic, lipids, antihistamines, laxatives, vitamins, decongestants, gastrointestinal sedatives, anti-inflammatory substances, antimanics, anti-infectives, coronary vasodilators, peripheral vasodilators, cerebral vasodilators, psychotropics, stimulants, anti-diarrheal preparations, anti-anginal drugs, vasoconstrictors, anticoagulants, antithrombotic drugs, analgesics, antipyretics, hypnotics, sedatives, antiemetics, antinauseants, anticonvulsants, neuromuscular drugs, hyperglycemic and hypoglycemic agents, antivirals, antineoplastics antidepressants, anticholinergics, antiallergic agents, antidiabetic agents, antiarrhythmics, antihormones, antihistamines,  $\beta$ -blockers, cardiac glycosides, contraceptives, contrast materials, radiopharmaceuticals, dopaminergic agents, lipid-regulating agents, uricosurics, tranquilizers, thyroid and antithyroid preparations, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, microorganisms, viruses, releasing factors, growth factors, hormones, antihelmentics, steroids, and mixtures thereof.

30. The implant composition of Claim 29 wherein said biologically active composition comprises a steroid, a hormone or mixtures thereof.

31. The implant composition of claim 30 wherein said biologically active composition comprises melengestrol acetate, a combination of melengestrol acetate and trenbolone acetate or a combination of melengestrol acetate, trenbolone acetate and estradiol.

32. The implant composition of Claim 31, wherein the melengestrol acetate is contained in each delivery vehicle in an amount of from about 5 to about 200 mg per delivery vehicle.

33. The implant composition of claim 26 wherein either component (a) or component (b) or both further comprises one or more of the following materials: standard granulating aids, lubricants, diluents, binders and glidants, magnesium stearate, stearic acid, colloidal silicon dioxide, talc, titanium dioxide, magnesium, calcium and aluminum salts, lactose, cyclodextrins and derivatives thereof, starches, povidone, high molecular weight polyethylene glycols and derivatives thereof, bioerodible polymers and co-polymers, polystearates, carboxymethyl cellulose, cellulose, N,N-diethylamine acetate, polyvinyl alcohol, hydroxypropyl methyl cellulose, other biologically active or inactive substances or other pharmaceutically active or inactive substances.

34. An implant composition consisting essentially of:

(a) a first component comprising melengestrol acetate contained in one or more pellets or tablets capable of immediately releasing said melengestrol acetate upon implantation in an animal body, said pellet or tablet containing a disintegrating agent; and

- 5 (b) a second component comprising melengestrol acetate contained in one or more pellets or tablets capable of releasing said biologically active composition on a sustained basis upon implantation in an animal body, said pellet or tablet not containing a disintegrating agent;

wherein said implant composition is implanted in an animal body by injection.

10 35. The implant of claim 34 consisting essentially of one to four pellets of type (a) and four to six pellets of type (b) which is administered by a single injection.

15 36. A method for delivering the same biologically active material to an animal body in both a rapid release and sustained release form comprising the steps of:

(1) providing an implant comprising:

20 (a) a first component comprising a biologically active composition contained in a first delivery vehicle capable of immediately releasing said biologically active composition upon implantation in an animal body and which is selected from the group consisting of encapsulants where the coating wall material is highly soluble in body fluids, porous or freeze-dried solid compositions, solid tablets or pellets containing a disintegrating agent which causes the solid tablet or pellet to rapidly break down when in body fluids, solid tablets or pellets containing said biologically active material in fine or micronized particle sizes, an osmotic delivery system where the osmotic system is such that a substantial amount of the active is released upon implantation and mixtures thereof; and

30 (b) a second component comprising the same biologically active composition as in component (a) contained in a second delivery vehicle capable of releasing said biologically active composition on a sustained basis upon implantation in an animal body and which is selected from the group consisting of encapsulated solutions or suspensions, biodegradable solid substances, conventional tablet/pellet ingredients, conventional tablet/pellet ingredients coated with a polymeric membrane to control release, conventional tablets or pellets containing said biologically active material

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5 having large particle sizes, matrix-tablets based on gel-forming excipients, matrix-type systems based on non-biodegradable polymers, membrane-type systems based on non-biodegradable polymers, matrix-type systems based on biodegradable polymers, matrix-type systems implant based on lipidic excipients, mass transfer systems based on osmotic pressure pumping through a hole in an impermeable coating and mixtures thereof; and

(2) injecting said implant into the animal body.

10 37. The method of Claim 36 wherein the first delivery vehicle comprises solid tablets or pellets containing a disintegrating agent and wherein the second vehicle comprises solid tablets or pellets not containing a disintegrating agent.

38. The method of Claim 37, wherein said disintegrating agent is selected from the group  
15 consisting of sodium crosscarmellose, microcrystalline cellulose, sodium carboxymethyl-cellulose, alginic acid, starch, potassium polacrilin, colloidal silicon dioxide, crospovidone, guar gum, magnesium aluminum silicate, methyl cellulose, powdered cellulose, pregelatinized starch, sodium starch glycolate and sodium alginate and mixtures thereof.

20 39. The method of Claim 36, wherein said biologically active composition is selected from the group consisting of enzymes or other organic catalysts, ribozymes, organometalics, proteins and glycoproteins, peptides, poly(amino acids), antibodies, nucleic acids, steroids, antibiotics, antimycotics, anti-narcotics, cytostatics, cytotoxics, cytokines, carbohydrates, oleophobic, lipids, antihistamines, laxatives, vitamins, decongestants, gastrointestinal sedatives, anti-inflammatory substances, antimanics,  
25 anti-infectives, coronary vasodilators, peripheral vasodilators, cerebral vasodilators, psychotropics, stimulants, anti-diarrheal preparations, anti-anginal drugs, vasoconstrictors, anticoagulants, antithrombotic drugs, analgesics, antipyretics, hypnotics, sedatives, antiemetics, antinauseants, anticonvulsants, neuromuscular drugs, hyperglycemic and hypoglycemic agents, antivirals, antineoplastics antidepressants, anticholinergics, antiallergic agents, antidiabetic agents, antiarrhythmics,  
30 antihormones, antihistamines,  $\beta$ -blockers, cardiac glycosides, contraceptives, contrast materials, radiopharmaceuticals, dopaminergic agents, lipid-regulating agents, uricosurics, tranquilizers, thyroid and antithyroid preparations, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, microorganisms, viruses, releasing factors, growth factors, hormones, antihelmentics, steroids, and mixtures thereof.

35 40. The method of Claim 39 wherein said biologically active composition comprises a steroid, a hormone or mixtures thereof.

41. The method of Claim 40 wherein said biologically active composition comprises melengestrol acetate, a combination of melengestrol acetate and trenbolone acetate or a combination of melengestrol acetate, trenbolone acetate and estradiol.

5 42. The method of Claim 41, wherein the melengestrol acetate is contained in each delivery vehicle in an amount of from about 5 to about 200 mg per delivery vehicle.

43. The method of Claim 36, wherein said animal is selected from the group consisting of cows, horses, sheep, swine, dogs, cats and humans.

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44. The method of Claim 43, wherein said animal is a heifer.

45. The method of Claim 36 wherein said implanting step is selected from the group consisting of subcutaneous, intramuscular, intraperitoneal, and intracranial injections.

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46. The method of Claim 45 wherein said animal is a heifer and said implanting step comprises subcutaneous injection in the posterior of the ear of said heifer.

47. The method of Claim 13 wherein step (2) comprises a single injection.

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